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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 18

Application Number: 09/324,465
Filing Date: June 02, 1999
Appellant(s): GLUCKSMANN ET AL.

W. Murray Spruill
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 13 July 2001.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is deficient because Appellants characterization that the "2841 receptor is a member of a family of proteins that are known in the art for their importance as therapeutic targets" is inaccurate since no such evidence has yet been provided.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 2, 9-14, 18-20, 22-30, and 33-37 do stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Berendsen. "A Glimpse of the Holy Grail?" Science, vol. 282 (23 October 1998), pages 642-643.

Galperin et al. "Who's your neighbor? New computational approaches for functional genomics" Nature Biotechnology, vol. 18 (June 2000) pages 609-613.

Attwood "The Babel of Bioinformatics" Science, vol. 290 (20 October 2000), pages 471-473.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 2, 9-14, 18-20, 22-30, and 33-37 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The claimed invention is drawn to an antibody specific for SEQ ID NO: 1, a method of screening agents which modulate the activity or expression of SEQ ID NO: 1 and variants and fragments of SEQ ID NO: 1, and methods of treatment using said agents or antibodies.

The specification discloses the cloning and sequencing of an open reading frame, namely SEQ ID NO: 2, which when translated, displayed some homology with a G-protein coupled receptor (GPCR), based on the presence of seven transmembrane domains and a DRY triplet, which is allegedly a GPCR motif. Moreover, the specification discloses that the cloned GPCR shares a high score with the seven transmembrane domain rhodopsin family. The specification, as filed, does not provide any evidence or guidance suggesting the claimed protein's activity or that mis-expression of the claimed

proteins are involved in any particular activity or disease state. Although the specification prophetically asserts using the claimed nucleotide sequences and its encoded proteins in various protocols such and recombinant technology, hybridization, antisense inhibition, chromosomal mapping, pharmaceutical compositions to treat diseases, etc..., no evidence or guidance is provided that would suggest to a skilled artisan that there is any utility in using any of the nucleotide sequences or its encoded proteins in the asserted protocols since applicants have not adequately described any specific activity for the alleged GPCR, thereby, casting doubt on whether the nucleotide sequence or its encoded protein can be used in any of applicants asserted utilities.

Additionally, the specification's lack of a specific and substantial asserted utility or a well established utility if further supported by applicants specification which notes that GPCRs are classified into five families with distinct activities, namely, I) beta2 adrenergic receptors, II) parathyroid hormone/calcitonin/secretin receptors, III) metabotropic glutamate receptors, IV) CAMP receptors, and V) fungal mating pheromone receptors, all of which have divergent activities. Moreover, the specification notes that proteins with putative seven transmembrane domains, much like applicants, are not necessarily GPCRs such as *boss* and *fz* cloned from Drosophila. Further compounding the accurate activity prediction of the claimed protein is that a protein's activity cannot be predicted based on primary structure alone, which is evidenced by Berendsen who teaches that "folding to the stable native state has not yet occurred, and the simulations do not contain any relevant statistics on the process" (page 643, second column). Further supporting Berendsen's teaching of unpredictability of activity

prediction based on homology, Galperin et al. teach that "sequence comparison methods, even the best ones, are of little help when a protein has no homologs in current databases or when all database hits are to uncharacterized gene products". Furthermore, Galperin et al. disclose "assessing the actual power of the context-based method for protein function prediction requires extensive testing by labor-consuming, case-by-case computational, and eventually experimental analysis".

Therefore, as discussed above, neither the art nor the specification as filed provides a specific and substantial asserted utility or a well established utility for the claimed nucleotide or amino acid sequences thereby casting doubt on the utility of the claimed antibodies and methods for agent screening and treatment as well as their asserted utilities. Lastly, since there was no specific and substantial asserted utility or a well established utility for the disclosed nucleic acids and encoded proteins, credibility of the utility was not assessed.

Claims 2, 9-14, 18-20, 22-30, and 33-37 are also rejected under 35 U.S.C. 112, first paragraph.

(11) Response to Argument

From the outset, it is noted that Appellants have not addressed the provisional obviousness-type double patenting rejection, that was made of record in the Office action mailed 25 August 2000, paper no. 8, in the instant Appeal Brief. Moreover, Appellants, in the response filed 4 December 2000, paper no. 9, have indicated that upon issuance of a Notice of Allowance, "[a]pplicants will file a terminal disclaimer in

compliance with 37 C.F.R. 1.321(c) to overcome this double patenting rejection", thus it is presumed that Appellants will file a terminal disclaimer to obviate the provisional obviousness-type double patenting rejection if the application should receive a favorable disposition from the Board of Patent Appeals and Interferences.

Appellants assert that the claimed 2871 polypeptide contains high sequence homology to the seven transmembrane receptor domains of the rhodopsin family of G-protein coupled receptors (GPCR) and further contains a DRY triplet at residues 138-140 of SEQ ID NO: 1 (Figures 2 and 3). Upon review of said figures, it appears that Figure 2 only shows a DRY triplet and Figure 3 shows the presumptive structures of the cloned polypeptide. Further, it appears that Figure 4 shows the seven transmembrane domains as discussed by Appellants. Although Appellants have indeed performed several structural analyses as discussed said analyses based solely upon structural comparisons is not sufficient to establish that the cloned polypeptide, 2871, is indeed a a GPCR as was stated in the instant rejection. Moreover, a cursory review of the sequence comparison in Figure 2 does not provide for the asserted high homology with the rhodopsin family of GPCRs. In fact, it appears that Figure 2 provides for only the DRY triplet and low sequence homology. In a recently published review concerning bioinformatics, Attwood notes that "[i]f the best hit in a database search is a match to a sigle domain or module, it is unlikely that the function annotation can be propagated from the parent protein to the query sequence" and "[t]he presence of a module tells little of the function of the complete system; knowing most components of a mosaic

does not allow us easily to predict a missing one, and modules in different proteins do not always perform the same function" (page 472, second column, first and second full paragraphs, respectively) thus supporting the assertion that protein function cannot be ascertained from analysis of its components, in this case the presence of seven transmembrane regions and a DRY triplet.

Although Appellants have performed various computer modeling and sequence comparisons with the 2871 polypeptide, said comparisons do not equate the claimed polypeptide with a GPCR as was supported by the cited references, Berendsen, Galperin, and Attwood. Furthermore, Appellants attempted comparison of the claimed 2871 polypeptide with the DNA ligase example of the published utility guidelines (http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf; 21 December 1999; example 10) is not found persuasive since the DNA ligase set forth in the example has a substantial and very specific utility that is well accepted in the art as opposed to Appellants' 2871 polypeptide. Appellants' 2871 polypeptide, allegedly a GPCR, is asserted to possess many functions as was set forth in the utility rejection. If, for arguments sake, we accept applicants assertion that the 2871 polypeptide is a GPCR, the specification still does not provide for a substantial or specific utility since GPCRs are grouped in a very large family of proteins having a multitude of functionally distinct activities as Appellants have admitted in the instantly filed specification and Appendix E. Such activities include I) beta2 adrenergic receptors, II) parathyroid hormone/calcitonin/secretin receptors, III) metabotropic glutamate receptors, IV) CAMP

receptors, and V) fungal mating pheromone receptors. Appellants have not associated any particular utility with the 2871 polypeptide other than asserting that it is a GPCR.

Appellants further assert that others, skilled in the art, have used such methodologies to characterize proteins and later confirm the asserted activity. For instance, Nguyen et al (Appendix B), Dickmen (Appendix C), and Kliewer et al. (Appendix D), as cited by Appellants, all disclose characterization of novel proteins based upon initial homology studies with sequence databases. Although such methodologies are acceptable means of beginning initial studies of a cloned polypeptide, it is clear that further experimentation and evidence was required from said authors to confirm their respective activities and thus their specific utilities. For instance, Nguyen et al. clearly notes that histamine receptors have proven difficult to identify since they share low homology with each other and in fact share higher sequence identities with other aminergic receptors (page 427, first paragraph). Dickmen teaches that in addition to the sequence homology with p53, the p73 gene is deleted in certain cancers thus providing additional evidence of its function. Lastly, Kliewer et al. teaches that the PXR.2 gene is identical to a characterized PXR.1 gene except for a 41 amino acid deletion resultant from alternative splicing. Thus, the cited references clearly provided additional evidence to confirm their findings in addition to the sequence homology studies.

Appellants further assert that Berendsen is directed to predicting the conformation of a protein's structure and not to its activity but it is noted that the activity of any protein or polypeptide is dependent upon its structure. Moreover, Appellants

assert that Galperin is not relevant since it is directed to comparisons to uncharacterized polypeptides or proteins as opposed to GPCRs which are characterized. Although their are many characterized GPCRs known in the art, Appellants have not provided any reasonable correlation between the cloned 2871 polypeptide and the characterized GPCRs as cited in Appendix E.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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August 25, 2001

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